EXHIBIT A

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

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IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: ***Susan Guinn v Ethicon, Inc., et al*** ***Case No. 2:12-cv-01121***	

EXPERT REPORT - TVT-O Guinn MDL Wave 1 Case

Stanley Zaslau, MD, MBA, FACS

This report summarizes my qualifications, training and experience, and my general and my opinions about the Guinn case. My opinions are based on the information I have reviewed as of the date of this report. If I receive additional information before trial, I may form additional or modified opinions. All of my opinions are expressed to a reasonable degree of medical and scientific certainty or probability and are based on my education, training, experience, professional society guidelines, analyses, position statements and medical literature, medical records, the TVT-O IFUs and Patient Brochures, depositions and other materials I have reviewed, as summarized in the attached reliance list. I have also reviewed the Expert Reports submitted by plaintiffs' experts. Exhibits that may be used to illustrate and support my findings are referenced herein and/or included in the literature and documents from my attached reliance list.

I. Background, Training and Experience

I received my undergraduate degree in biology and psychology from Boston University in 1988. I attended Hahnemann University School of Medicine and received my MD degree in 1994. I completed my internship in general surgery and urology residency training at Mount Sinai Medical Center (New York) in 2000. I completed an additional year of training as part of the Consortium Group Urologic Surgical Associates in Brooklyn, New York, where I received advanced training in incontinence, voiding dysfunction, prosthetics and pelvic prolapse.

Upon completion of training in 2001, I accepted a position as Assistant Professor of Urology at West Virginia University. My practice area of focus was incontinence and voiding dysfunction. I achieved board certification in urology in 2003. I was promoted to Urology Residency Program Director and Associate Professor of Urology in 2005. I was promoted to Professor and Chief of the Division of Urology in 2010.

In 2013, I took and passed the inaugural subspecialty certification examination in Female Pelvic Medicine and Reconstructive Surgery and was the first such certified professional in the State of West Virginia. In 2013, I was named as the Associate Chairman of Education and Research for the Department of Surgery. My practice is still very active in incontinence, voiding dysfunction and sexual dysfunction in men and women. I serve as the Co-Director of the West Virginia University Center for Voiding and Sexual Dysfunction.

I am very active in the practice of incontinence, voiding dysfunction and pelvic floor prolapse. I learned to perform the retropubic TVT procedure in residency (1996-2000) and was able to appreciate the ease of performing this procedure. I was also taught how to perform pubovaginal slings and came to appreciate the added morbidity associated with the abdominal approach to harvest fascia for these cases. Vaginal wall suspensions were also commonly performed during that time and their failure rates and complications of suture erosion and extrusion were also well appreciated by me.

During my year of advanced training, I assisted and performed many retropubic TVT procedures without any intraoperative complications and excellent post-operative results.

From 2001 to the present time, I have performed hundreds of TVT procedures, including TVT and more commonly the TVT-O type. Although the TVT is still available at our facility, we commonly use the TVT-O procedure because it is efficient, efficacious and has a lower incidence of potential bowel injuries than the traditional retropubic TVT. I still consider the traditional TVT as part of our armamentarium of suburethral sling options for women with stress urinary incontinence. I am very familiar and comfortable with both retropubic and obturator synthetic midurethral sling procedures and have had excellent success with them. I have not had any bowel, bladder or vascular injuries. I am also comfortable and routinely perform pubovaginal slings (autologous and cadaveric fascia) as indicated or as desired by patients. I carefully review with patients preoperatively, postoperatively and at each subsequent office visit all of the known risks and potential complications of pelvic floor surgery including incontinence, recurrence, voiding dysfunction, pain, sexual dysfunction, mesh erosion and extrusion. This has resulted in excellent long term patient satisfaction over 15 years.

A copy of my C.V., which sets out my training, education and experience and my publications, is attached. I am being compensated for my work in this matter at a rate of $500 an hour. For work required to be turned around in 10 days or less, my rate increases to $750 an hour. Depositions and appearances at trial follow a different fee schedule. I have given depositions and testified at trial as an expert witness a few times in the past four years.

II. Summary of Opinions

A summary of my opinions, as set forth in more detail later in this report, is as follows:

- Many women suffer from urinary incontinence, including stress and urge incontinence. Incontinence can be very detrimental to a woman's quality of life.
- There are non-surgical options for the treatment of stress urinary incontinence. However, non-surgical options are not always effective and many women ultimately seek surgical treatment after first considering or trying non-surgical treatments.
- Surgical options include Burch colposuspension and sling procedures, consisting of either autologous fascia, cadaveric tissue, materials of other biologic origin, or macroporous, monofilament polypropylene. For many patients, surgery is the most effective treatment for stress urinary incontinence.
- Polypropylene mid-urethral slings like the TVT and TVT-O are widely recognized as the standard of care for treating SUI today. They have been extensively studied and authoritative professional organization statements and the medical literature endorse and recommend their worldwide use by physicians in clinical practice which reflect their utility to surgeons and usefulness to patients in the overall surgical armamentarium.
- The TVT-O sling system used in this case is one that I have used in my own clinical practice for many years in hundreds of patients. It is safe and

effective as a treatment for SUI and is less invasive than other surgical treatments.

- All surgeries have risks, and surgeries for the treatment of SUI are no exception. The main risks associated with sling procedures are taught to surgeons in training, are discussed at professional conferences and are widely reported in the medical literature.
- Pelvic pain, dyspareunia and other pain is frequently found in women of various ages and in the general background populations. The causes are multiple, such as other medical conditions like interstitial cystitis, dysmenorrhea, prior surgery, musculoskeletal dysfunction, estrogen status and tissue pliability. The medical literature and my clinical experience demonstrate that many women presenting for urologic and gynecologic conditions, such as prolapse and incontinence, have these complaints at baseline.
- Urinary incontinence and pelvic floor prolapse can be associated with sexual dysfunction. Affected patients can complain of difficulty with sexual desire, arousal, orgasm, lubrication, pain and satisfaction.
- Risk factors for female sexual dysfunction include: post-menopausal status, degree of pelvic prolapse, concurrent medical problems such as hypertension, diabetes and thyroid disease, surgical menopause from hysterectomy and scarring from prior episiotomy and repair of tears during childbirth.

- Pelvic pain and other pain (inguinal and lower extremity related pain) are known risks of sling procedures (or any other vaginal surgery). However, pelvic pain, dyspareunia, and other sexual function factors such as fear of sex from incontinence, can also improve after sling procedures.
- The warnings provided in the TVT-O IFU were appropriate and sufficient to provide surgeons with sufficient information about the product. It is the responsibility of any surgeon to ensure that the patient understands the potential risks and benefits of a procedure. As noted in the IFU, leg pain may occur, but the medical literature and my clinical experience have found persistent leg/groin pain to be rare with the TVT-O. In fact, studies comparing the TVT-O to the TVT-Abbrevo have shown no difference in leg/groin pain after the immediate post-operative period. The professional education provided by Ethicon was comprehensive and well-designed. The vast body of medical literature provides surgeons with the appropriate resource for understanding the frequency and severity of complications associated with TVT, TVT-O, and other pelvic floor procedures, as well as managing complications.
- Decisions regarding the best treatment for SUI are made by a woman and her doctor. Mrs. Guinn consented to the procedure after discussing her treatment options with Dr. Cooper.
- Dr. Cooper was aware of the risks and complications associated with the TVT-O procedure and according to his testimony and the medical record,

he discussed those risks and potential complications with her in detail and gave her the opportunity to ask any questions.

- Long-term studies evaluating TVT-O have shown that severe complications are acceptably low and that the TVT-O is a safe and effective procedure for women with SUI.
- Pain, sexual dysfunction, dyspareunia, and voiding problems are complications associated with any pelvic floor procedure, including vaginal hysterectomies, bilateral salpingo-oopherectomies, and anterior repairs.
    - Mrs. Guinn was found to have a tight urethra and vaginal shortening on examination. It has been reported that patients undergoing TVH and prolapse repair can have a 2 cm decease in vaginal caliper and increased dyspareunia (Abdelmonem, 2010).
    - Mrs. Guinn had recurrent UTI both preoperatively and post operatively. According to the Plaintiff Fact Sheet, she noted "frequent UTIs, urinary retention which required urethral dilation." This along with post operative voidjng dysfunction (as noted on Mrs. Guinn's ultrasound which would explain why she was dissatisfied with her sling procedure. These two factors were noted by Groutz (2011) as reasons for subjective failure of retropubic TVT.
    - When additional surgical procedures are combined into a single operation (Vaginal hysterectomy + pelvic floor reconstruction +

TVT sling), the subjective failure rate of the TVT is highest when all procedures are performed together. In 2010, Mrs. Guinn underwent TVLH, BSO, anterior repair and TVT-O sling.

- Mrs. Guinn stated in her MDL case information that she had problems related to the device that included "pain." Of note is that in the office notes from practitioners she has seen on 4/14/10, 7/20/10, 7/26/10, 11/15/10, 12/6/10, 1/20/11, 7/6/11 and 9/24/14 that she did not mention having pain to any of the practitioners that she saw.
- Mrs. Guinn in her deposition notes that she was given a brochure that discussed the sling surgery she was supposed to have including the sling procedure and the hysterectomy. She believes that Dr. Cooper explained the risks of these surgeries as he knew them and would not dispute that he did so. She does not remember signing the consent form for the proposed surgery.
- Mrs. Guinn in her deposition is not descript about her problems being related to the mesh as she herself attributed them to the mesh after seeing a commercial on TV in 2011. She described having recurrent UTIs but is "not sure how many" and describes pulling in the groin as pain that "happens once in a while." Further, she has not spoken with her physicians about this pain because "….I guess I have it, then I don't have it (pain)" She takes no precautions to

prevent UTI and states that "…I am not aware of anything to do," but drinks a lot of water.

- Dr. Cooper states that he gave a brochure to the patient regarding TVT. At the time of Mrs. Guinn's procedure, the brochure reflected current issues with sling procedures including voiding dysfunction, and pain with sexual intercourse.

- Since my arrival at WVU in 2001, a comprehensive educational and training program to teach the medical and surgical aspects of incontinence has been developed and maintained.
- As the first subspecialty boarded certified physician in Female Pelvic Medicine and Reconstructive Surgery, I have been able to provide care for, instruction in and surgical training in all aspects of this discipline.
- Residents and faculty at all Urology and Ob/Gyn residency training programs have received some of my didactic lectures in this evolving discipline.
- Instruction on the TVT and TVT-O's indications, procedural specifics and contraindications has been taught to residents in Urology and Ob/Gyn at WVU since my arrival in 2001. This synthetic midurethral sling (both retropubic and transobturator) represents a core treatment for stress urinary incontinence and must be understood by all resident trainees.
- Because the synthetic midurethral sling is considered to be the gold standard, or standard of care treatment for stress urinary incontinence, practicing West Virginia Urologists and Ob/Gyn physicians are not only

facile in TVT-O use but have routinely performed these procedures since its inception. Didactic knowledge and updates on its use in practice are discussed routinely at state meetings in which I have presented lectures at.

- Residents also receive didactic teaching and surgical instruction in the performance of cadaveric and autologous pubovaginal slings. They come to appreciate the more challenging nature of this procedure and its associated intraoperative and postoperative complications (particularly the significantly increased postoperative pain and voiding dysfunction).

IV. Opinions

A. Urinary Incontinence

Urine is produced by the kidneys and flows via peristalsis down the ureter to the bladder. Urine is then held in the bladder until voiding is undertaken. The urethra is at the most distal end of the urinary tract. Urine passes from the bladder through the urethra.

Urinary incontinence occurs when there is an involuntary loss of urine. This condition can be progressive, with significant worsening of symptoms over time. There are several types of urinary incontinence, namely urge incontinence, stress incontinence and mixed incontinence.

Urge incontinence is the involuntary loss of urine associated with increase in bladder pressure. The pressure increases to the point where voiding cannot be deferred and wetting accidents occur. The etiology of urge incontinence can be idiopathic or neurologic and also has significant associations with dietary intake.

Stress urinary incontinence ("SUI") is the sudden involuntary loss of urine in association with exertion, coughing, sneezing or other activity or movement.

If a patient has both urge incontinence and SUI she is described as having **mixed incontinence**.

Many factors have been associated with SUI. Risk factors include obesity, age, parity, vaginal delivery, menopausal status, diabetes, family history and history of hormone replacement therapy. Physical activity and smoking may also be risk factors. SUI may occur with injury or degeneration to the urethral support system or urethral sphincter mechanism; it is more likely that most women have elements of both problems. Women with a cystocele may have urethral hypermobility but not necessarily stress incontinence. If they have stress incontinence, they may have some urethral sphincter compromise along with the hypermobility. Trauma from obstetric delivery or another traumatic experience has been implicated in causing stress incontinence. Meyer and colleagues (1998) studied patients during pregnancy and 9 weeks postpartum. They found that 36% of women who were delivered by forceps and 21% who delivered spontaneously suffered from urinary incontinence. Bladder neck mobility was significantly increased after all vaginal births, but bladder neck position at rest was only lowered in the forceps group. In addition, bladder neck mobility was significantly increased after all vaginal births, but bladder neck position at rest was only lowered in the forceps group. Women who underwent cesarean delivery were unaffected Levator ani injuries can also occur after childbirth and result in later pelvic floor prolapse.

Stress urinary incontinence is common and is estimated to occur in approximately 1 of 3 women. Dooley and associates (2008) reported that half of women

over age 20 complained of incontinence symptoms. In this study, nearly 50% of patients reported pure SUI whereas 34% complained of mixed urinary incontinence. Nyygard and colleagues (2008) and Wu and associates (2010) reported that the prevalence of SUI increases with age. According to an AUA Foundation report in 2011, fewer than 50% of patients who suffer from incontinence report this to their healthcare provider and this may be due to embarrassment and shame. This is very unfortunate, because urinary incontinence can have a profound negative impact on women's well-being. Patients may experience isolation, limitation of social activities, professional limitations in terms of job advancement/promotion as well as impair intimate relationships. Patients may refrain from beneficial activities such as exercise because of fear of urine leakage. Wu and colleagues (2014) estimated that the lifetime risk for a woman to have surgery to treat SUI is 13.6%. Bing and associates (2015) described clinical risk factors in terms of mixed urinary incontinence, previous incontinence surgery, body mass index greater than 35, age greater than 75, and presence of diabetes as significantly related to a less successful outcome of incontinence surgery.

The AUA guidelines were initially created in 1997 and revised in 2005, 2009 and 2012 to assist clinicians in the diagnosis and treatment of stress incontinence. The guidelines also suggest the importance of diagnosing concomitant pelvic prolapse as this can influence the modality of treatment selected for each patient. Evaluation and symptoms assessment must be undertaken for each patient including demonstration of incontinence with increasing abdominal pressure, frequency of urination, the severity of symptoms and degree of bother, the function of the urethral sphincter and the degree of hypermobility. Each patient should have a focused history to ascertain the type of

incontinence present as well as the frequency bother, severity of symptoms and impact of symptoms on lifestyle. Further discussion should focus on the patient expectations of treatment. Physical examination with objective demonstration of stress urinary incontinence is mandatory. Formal urodynamic evaluation may be of assistance in patients with complex presentations of incontinence such as the patient with mixed urinary incontinence. Patients must be counseled about comorbidities that can affect treatment outcomes. This allows the physician to plan an individualized treatment plan, obtain an informed consent, project an estimate for a successful outcome and list potential complications.

B. Treatment Options for Stress Urinary Incontinence

Once diagnosed, the options for treatment of SUI include behavioral therapy or lifestyle changes, nonsurgical treatment and surgical treatment. Behavioral therapies include bladder training, fluid and diet management, smoking cessation, weight loss, avoiding bladder irritants and scheduled toilet trips. Nonsurgical options include Kegel exercises and the use of a pessary (a device inserted into the vagina to support the pelvic area and urethra). Kegel exercises are patient-taught exercises to identify the muscles of the pelvic floor that are involved in maintaining urinary continence. Patients are taught to squeeze and relax these muscles several times each hour, several times per day. When conducted over the long term, patients can see a modest improvement in urinary incontinence symptoms. However, success with Kegel exercises requires a motivated patient. Thus, there is a significant drop out rate for this therapy and many patients will go on to require additional therapies.

Pessaries are silicon, non-allergic devices that are placed into the vaginal canal to reduce pelvic floor prolapse. In general, these are used in patients with pelvic floor prolapse. Some patients with prolapse also complain of urinary incontinence. Pessaries can be considered for these patients. There is no difference between the types of pessary used when looking at patient satisfaction with this therapy. Pessaries need to be removed periodically to be cleaned and are then replaced. Many patients with pessaries drop out from this therapy because it is cumbersome and requires quite a bit of follow up care. The index patient to consider a pessary for is one with significant pelvic floor prolapse who is a poor surgical risk because of multiple medical problems. It is most successful in the elderly patient.

Usually, nonsurgical or behavioral options are helpful only in milder cases of urinary incontinence, and only provide a lasting cure in a small subset of patients. For example, while many women experience some improvement from Kegel exercises, in my clinical experience few find this to be a permanent solution. Similarly pessaries are not convenient and can lead to vaginal discharge, pain, odor or bleeding. Many women discontinue pessaries or other similar nonsurgical treatments.

Biofeedback with pelvic floor muscle therapy teaches patients to identify muscles in the pelvic floor that are responsible for bladder and bowel continence. Through identification of these muscles, patients learn to control muscle function and possibly improve continence. This modality requires periodic therapy visits lasting approximately 30 minutes in duration for a several week cycle. Some improvement in urinary incontinence is noted for the motivated patient in the short term. Biofeedback can also be combined with electrostimulation of the pelvic floor muscles and short-term

studies show limited benefit through this additive therapy. However, with biofeedback (with or without electrostimulation), there is a significant dropout rate from treatment and many patients will go on to other therapies.

Bulking agents like collagen are sometimes used to treat SUI. In this treatment, the agent is injected into tissues around the upper portion of the urethra via a cystoscope. This is not a permanent repair and is not as effective as surgery.

Surgery is the most effective and definitive way to treat SUI. Surgical options include colposuspension and sling procedures consisting of either rectus fascia or fascia lata from the patient, cadaveric or biologic tissue, and macroporous, monofilament polypropylene used in the TVT.

The Burch colposuspension is an invasive surgical procedure involving an abdominal incision and identification of the pelvic bony ligamentous structures. Sutures are placed into the periurethral tissue and into the bony ligamentous structures. The long-term success rate for the Burch procedure is approximately 50-60%. Galloway (1987) reported their experience with Burch procedures. Continence was achieved in only 42 patients (approximately 50% of all patients). Although all but one patient without previous surgery became continent, only 12 of 19 patients who had undergone previous surgery were continent post-operatively and five of the seven who showed little or no improvement had had at least two previous procedures for incontinence. They reported an unacceptable number of post-procedural complications including: persistent incontinence, voiding difficulties, urge syndrome, post-colposuspension syndrome, uterine prolapse, enterocele, dyspareunia, and recurrent incontinence. Demirci (1991) studied the long-term complications of Burch procedures. They noted, at follow up, late

complications occurred in 220 women. These included cystocele in 18; rectocele in 32; enterocele in 35; dyspareunia in 6, and groin or suprapubic pain in 15. They noted that the cure rate of Burch colposuspension is satisfactory, although it declines with time. Alacay (1995) reported their long-term complications from Burch procedures. They noted post-operative complications including de novo detrusor instability in 15% of patients, long term voiding difficulty in 22% of patients and recurrent UTI in nearly 5% of patients.

Kjolhede (1996) studied the rate of prolapse after Burch procedures. They found on clinical examination a significant progression of rectoceles ($p=0.003$) after the colposuspension. Six women (29%) had subsequent corrective prolapse surgery within 2 years after the colposuspension. Parisio (2004) compared TVT to laparoscopic Burch procedures for stress urinary incontinence. They noted post operative symptoms of incontinence (stress, urge, and any urinary incontinence) were reported significantly more often in the laparoscopic Burch colposuspension group that in the TVT group. Kayan (2008) studied the effects of sexual function after Burch procedures when compared to vaginal slings. They noted that postoperative sexual function improved in 13 women (24.5%) of the vaginal sling group and in 5 women (12.2%) of the Burch colposuspension group, and remained unchanged in 15 (28.3%) and 10 (24.4%), respectively. Sexual function deteriorated in 25 (47.2%) of the sling group and 26 (63.4%) of the Burch group. They concluded that sexual function may be impaired after surgery for SUI. Burch colposuspension may deteriorate sexual function much more than vaginal sling surgery in women. Therefore, women who will need surgery for SUI should be informed of the risk of deterioration of sexual function after surgery.

Geller and colleagues (2013) described the dramatic shift over the past two decades as the synthetic midurethral sling has replaced the fascial sling and Burch colposuspension as the criterion standard for treatment of female stress urinary incontinence.

Albo and colleagues (2007) studied two groups of patients with SUI. They noted a success rate of 49% for Burch and 66% for fascial slings in patients with SUI. They noted that more women who had a fascial sling had UTIs, difficulty voiding and post-op urge incontinence. The Burch procedure because of its abdominal incision, usually requires an inpatient hospital stay and has complications of wound infection, urethral injury and voiding dysfunction. As discussed below, the TVT has become much more popular than the Burch procedure and fascial sling because of its high efficacy, low morbidity, less invasiveness and ease of use.

Other types of surgical procedures used in the past to treat SUI, such as the Marshall-Marchetti-Krantz procedure, anterior colporrhaphy and needle suspension procedures, are not used very often today and are not recommended as the standard of care by medical associations because of a lack of efficacy and/or their complication profile.

C. Urogynecologic Education in West Virginia: A 15 year evolution.

Since its approval in 1998, TVT has been performed in West Virginia. Between 1998 and 2001 few cases were performed at WVU and throughout the state simply because there was no physician in the urology or Ob/Gyn Departments that had a subspecialty focus on the surgical treatment of incontinence. In my discussions with practitioners present prior to my arrival, the few cases that were performed went well but since there was no specialist in incontinence, the patient volume was low. Since my

arrival at WVU in 2001, and through collaborative efforts with the Ob/Gyn Department, a significant increase in surgical volume was experienced and thus, the number of patients receiving TVT increased significantly. This increase was also noted at the local and regional level through my involvement in lectures on surgical management of incontinence at various hospitals and through CME lectures.

After completing my advanced training in Brooklyn in incontinence, voiding dysfunction, prosthetics and pelvic prolapse, I sought an academic position where I could further education, training and clinical practice in this discipline. Through my interview process at West Virginia University, I learned that they were very interested in developing clinical programs in this area. Further, as the only urology residency training program in the state, their vision was to further education on a regional and state level. They were interested in also interested in having me develop collaborative programs with other Departments including Obstetrics and Gynecology, Family Medicine and Internal Medicine. Finally, they wanted me to deliver lectures in my areas of specialty to physicians at local hospitals throughout West Virginia. The process has been on going and continues to the present time.

I enthusiastically accepted this challenge upon completion of training in 2001. I was appointed as Assistant Professor of Urology with a focus on incontinence and voiding dysfunction. My first task was build a collaborative clinical program entitled The Center for Voiding and Sexual Dysfunction at West Virginia University. Created in 2002, this program's goals were to care for the men and women suffer from sexual dysfunction, incontinence, bladder and prostate problems, chronic pelvic pain, or related

problems. This program is available to any practitioner throughout the state for their patients. A summary of this program is shown below:

> "Effective treatment for these complex conditions requires a knowledgeable team of specialists. WVU's Center for Sexual and Voiding Dysfunction brings together experts in urology and obstetrics and gynecology to provide the highest level of care in a team approach.
> Center specialists are experts in state-of-the-art medical and surgical treatments for sexual and voiding disorders. Depending on the diagnosis, options may include medication, surgery, or other treatments. Our physicians are experts in the latest minimally invasive techniques that can often provide relief with a maximum of comfort and convenience. The Center conducts research trials into the latest treatments, which are continually improving as knowledge in these areas grows.
> Information and Referrals
> To consult with one of the Center's specialists or refer a patient, call the Medical Access and Referral System at 800-WVA-MARS or 800-982-6277."

Through the Center, approximately 50 patients are seen per week with 10 new patient consultations. Patient satisfaction scores via Press-Gainey survey data show that the Center is in the top 1% in this area. In fact, in 2015, I received the WVU Healthcare Award for Highest Press Gainey Scores in the area of Patient Satisfaction. In addition, I was named a Top Regional Urologist by Castle Connelly for 2014 and 2015.

With the Center for Voiding Dysfunction up and running, attention was then turned toward development of comprehensive education for WVU Urology and Obstetrics and Gynecology Residents. In 2002, a dual clinical rotation in Urogynecology was developed for medical students and residents. All core areas of urogynecology are taught. Obstetrics and Gynecology residents take the rotation for one month each academic year of their training while urology residents receive ongoing education commensurate with their level of training. Executive summary of this teaching program are shown below.

Resident Rotation Overview:

The Urogynecology Rotation is administered under the auspices of the Department of Obstetrics and Gynecology and the Division of Urology. The following are goals and objectives of this rotation include an understanding of: Epidemiology of urogynecologic disorders, anatomy and physiology of voiding function and dysfunction, classification of voiding dysfunction, evaluation of urinary incontinence, endoscopy of the lower urinary tract, surgical and nonsurgical treatment of urinary incontinence, evaluation and management of fecal incontinence disorders, and surgical correction of pelvic prolapse. In addition, the core ACGME objectives of patient care, medical knowledge, practice based learning and improvement, interpersonal/communication skills, professionalism and systems-based practice are also covered during the rotation.

Residents are taught three core components of urogynecology including: clinical, didactic and surgical. Clinical urogynecology is taught by faculty members in the clinic setting. In the clinic setting, residents are responsible for the initial evaluation, diagnostic workup and follow up of patients. In the Urology clinic under the guidance of Dr. Stanley Zaslau, residents will see approximately 50 patients/week. In the Urogynecology Clinic Dr. Robert Shapiro, residents will see approximately 10-20 patients/week. Diagnostic procedures such as cystoscopy, urodynamics and anorectal manometry are performed in the clinic procedure room or in the 2 west urodynamics suite. Approximately 15 procedures are performed/week.

The didactic component of urogynecology consists of monthly lectures delivered by core faculty. Highlights of this curriculum include: Anatomy of Female Pelvic Support, Neuroanatomy and Neurourology, Urodynamic evaluation of the lower urinary tract, Urethral Diverticulum and Fistulae, Interstitial Cystitis, Geriatric Urinary Incontinence, Complications of Prolapse Surgery, Update on Slings, Female Sexual Dysfunction, Fecal Incontinence, Surgical Treatment of Anterior, Posterior and Apical Prolapse and Non Surgical Management of Urinary Incontinence. Lectures also include case presentations. The series repeats annually. There is a semiannual urogynecology journal club.

The surgical component of urogynecology is taught in the operating room. Residents are given increasingly more responsibility as their experience grows. All aspects of surgical urogynecology are taught including: Surgery for Anatomic Incontinence, Treatment of Intrinsic Sphincter Deficiency, Pelvic Prolapse, Trauma and Fistulae, and Sacral Neuromodulation. Intensive experience in urodynamics and diagnostic cystoscopy are also provided.
Upon completion of the rotation, residents are formally evaluated by supervising faculty members.

Formal listing of lectures to be covered in the Urogynecology Curriculum:

1. Complications of Pelvic Prolapse Procedures
2. Geriatric Urinary Incontinence
3. Fistulae and Diverticulum
4. Nonsurgical treatment of Incontinence
5. Update on Interstitial Cystitis
6. Female Sexual Dysfunction
7. Neurogenic Bladder and Urinary Tract Infections
8. Evaluation of Urinary Tract Function and Urodynamics
9. New Concepts in Sacral Neuromodulation
10. Update on Slings for Stress Incontinence
11. Case Presentations in Urogynecology
12. Role of Estrogen in Urogenital Atrophy
13. Update on Nephrolithiasis
14. Injuries to the Ureter
15. Urinalysis
16. Anatomy and Physiology of the GU Tract
17. Urogynecology Jeopardy

The curriculum has been overwhelmingly successful and receives extremely positive evaluations from residents. Because of this success, the Obstetrics and Gynecology Residency Programs in Charleston (Womens and Childrens Medical Center) and Huntington (Marshall University Medical Center) have invited me to lecture on some of these core topics periodically over the years. These lectures continue to the present time.

The education of practitioners in Female Pelvic Medicine and Reconstructive Surgery continues on the regional level for current practitioners in a variety of settings. CME sponsored lectures have been given at Clinics, Hospitals and Regional Medical Society Meetings (2002- present). Below is a listing of venues where I have taught topics in FPMRS:

Venues for Clinical Lectures in FPMRS (2002-present):

- Marshall University Department of Obstetrics and Gynecology, Huntington WV
- West Virginia Osteopathic Medical Society, Hurricaine WV
- Womens and Childrens Hospital – Charleston, WV
- Coordinated Ob/Gyn Society Meeting, Charleston WV
- Princeton Community Hospital, Princeton WV
- West Virginia Family Physician Meeting, Charleston, WV
- Princeton Ob/Gyn Partners, Princeton, WV
- Primary Care Network CME Conference, Charleston, WV
- Belmont Medical Society, Belmont OH
- Logan Area Medical Center, Logan, WV
- West Virginia Ob/Gyn Fellows Conference, Roanoke, WV

In 2013, I took and passed the inaugural subspecialty certification examination in Female Pelvic Medicine and Reconstructive Surgery and am currently one of three such certified professional in the State of West Virginia. This certification has resulted in a modification of the teaching curriculum to reflect the FPMRS Core Curriculum (2012). Timely lectures regarding the current status of Mesh use in the pelvic floor is a popular topic of lectures.

Didactic and surgical instruction on TVT is taught to Urology and Ob/Gyn residents as part of the FPMRS Core Curriculum. Residents need to understand the indications, contraindications, procedural steps and how to manage complications. During the last few years, fewer traditional TVT cases have been performed. The ease of performance of the TVT-O has led to a shift towards these procedures as the standard of care in the management of stress urinary incontinence in West Virginia. The obturator approach is easy to teach, and has lower risk of bladder, bowel and vascular complications. In our experience, the long term efficacy of traditional TVT and TVT-O are similar, we choose to perform more TVT-O procedures.

As part of the FPMRS Core Curriculum, instruction in other surgical procedures for stress urinary incontinence is taught so that residents are well versed in these procedures. The Burch procedure is still taught and performed on occasion for patients who desire (for personal or religious reasons) not to have mesh placed. Residents learn that these procedures take longer to perform, require an in patient hospital stay and in the long term have somewhat less efficacy than the TVT procedures. Similarly, residents receive clinical and surgical instruction in the performance of autologous and cadaveric fascial pubovaginal slings. A number of these procedures are performed annually for patients who desire (for religious or personal reasons) not to have mesh placed, or have had a prior mesh sling that was removed or was not efficacious. Residents learn that these procedures take longer to perform, have a higher rate of postoperative pain and urinary retention and have an inferior success rate to TVT procedures in the long term.

While instruction in all aspects of surgical management of stress incontinence is taught to residents (Burch, TVT, TVT-O, pubovaginal sling autologous or cadaveric fascia), our residents come to experience that the TVT procedure is the easiest to perform in the appropriate clinical situation and has excellent long-term efficacy. Residents are also taught to have candid discussions with patients regarding the potential risks of pelvic floor surgery and to follow up with their treating physician at least on an annual basis and more urgently if problems are to arise such as worsening incontinence, pelvic pain, urinary tract infection, sexual pain or feeling mesh in the vaginal wall.

Residents also receive instruction in the performance of abdominal sacral colpopexy surgeries. These mesh-based procedures are performed either robotically or

via the open abdominal approach. This procedure is an important part of their armamentarium for the patient who has failed a prior vaginal prolapse procedure and requires a second repair for their prolapse.

D. Reasonableness of the TVT-O's Design for its Intended Use and its Utility / Usefulness

TVT was initially introduced in 1998 as a minimally invasive way to treat SUI. This was needed because of the surgical challenges with Burch and Pubovaginal slings discussed above. Further, there were significant complications and lack of efficacy seen with needle suspension procedures (Raz Bladder Neck Suspension, Pledget-based needle suspensions and the four cornered vaginal sling). While short term (6-12 month) success was common with these procedures, longer term success was lacking. Further, there were significant complications noted with some of the procedures (Pledget-based needle suspensions) including erosion into the urethra and bladder. Thus, the need to invent a minimally invasive procedure was warranted. The TVT fulfilled this need by being minimally invasive and is easy to perform when indicated and when the guidelines specified by the manufacturers are followed accordingly. Patients certainly wanted a minimally invasive procedure that could treat their stress urinary incontinence and have them able to resume their usual daily activities with a short recovery period and periodic follow up with their physician to ensure that they were doing well.

The design is safe and the short/long term efficacy is certainly present. To date, I have never had injury to any nerve, bowel or bladder (other than incidental isolated recognized trocar injury to the bladder, easily treated with short term catheter

placement). TVT-O, which uses the same Prolene mesh as TVT, became available in 2004 as another tool in surgeons' toolkits to help treat incontinence with a reduced risk of perforating the bladder. In my experience I have had 3 cases of TVT mesh extrusion treated only with simple excision. My success rates are excellent and go out to 15 years with the use of TVT and TVT-O procedures with most patients dry or still significantly improved from pre-operative baseline.

TVT and TVT-O implantation are both technically easy to perform and easy to teach. The tape is fashioned under the urethra using small standard vaginal wall dissection that is only 1.5cm in length. This design is important because it involves minimal dissection to create a small tunnel for the sling to be placed into which follows the path of the urethropelvic ligament. As compared to the traditional pubovaginal sling, this dissection is quicker and easier to perform.

Explicit instructions via video and step by step instructions were provided by the manufacturer. Professional education courses were also provided by the manufacturer on how to safely perform this procedure. When I learned how to perform this procedure in residency, I viewed the videos, which carefully explained all the necessary steps of the procedure.

Emphasis was placed on positioning the tape under the midurethra in a tension free manner using a clamp or Hegar dilator behind the tape so it does not obstruct the urethra. A Babcock clamp can also be used and can be placed around one of the plastic trocars once it has been transected after being positioned and removed from its thigh exit point. This allows the mesh to be positioned at the mid urethra easily. The trocar is placed around the mesh in the midline and the Babcock maintains the position. This

prevent the mesh from being placed under tension or stretched. Any of the abovementioned techniques are considered to be a critical portion of the procedure and allows the sling to sit without tension so that over time its incorporation into the tissue planes will be such that it mimics the location of the normal urethropelvic ligament and minimizes urethral hypermobility during stress. This is a critical design feature that physicians who perform the procedure must pay careful attention to in order to limit potential adverse effects such as voiding dysfunction, urethral pain and urethral erosion.

The manufacturer's videos, IFU and subsequent articles by leading academic physicians have further reiterated this important concept. Instruction was also provided to slowly remove the plastic sheath to prevent shearing of the tape. This is well illustrated on the manufacturer's videos, and subsequent articles by leading academic physicians. It is well known that when the plastic tape is pulled quickly or is under excessive tension that the mesh can lose a few particles from the ends of tape. Such a reaction does not occur when used as designed. The sheath covering the mesh is easily removed when removed as instructed and the techniques described above are utilized to prevent the mesh from being placed under tension. Further, I have not seen any complications attributed to particle loss or mesh fraying in the hundreds of randomized controlled trials evaluating the safety and efficacy of TVT and TVT-O, nor have I had any problems or complications associated with particle loss from TVT-O in my practice. Likewise, there are no reliable scientific studies evaluating the TVT or TVT-O that have demonstrated any clinical significance to alleged cytotoxicity, degradation, or cancer. Dr. Rosenzweig's opinions are founded on unreliable information lacking any valid scientific methodology. My clinical experience is consistent with the peer-reviewed level

1 clinical evidence in that there is no causal link of TVT-O to cancer or any other complication attributed to particle loss or degradation.

Synthetic slings are the most common type of surgical procedure performed today for SUI and monofilament, large pore polypropylene used in TVT is the most common type of synthetic material used in slings. Slings have a number of advantages over the Burch colposuspension procedure. In that procedure, the vaginal wall is attached to the Cooper's ligament adjacent to the public bone. A longer hospital stay is required. Surgical times and recovery times are longer. Patients often leave the hospital with an indwelling urinary catheter. Wound complications and hernia can occur. While the laparoscopic Burch is considered to be less invasive than the open Burch, it is more difficult to learn and perform, must be performed under general anesthesia, requires multiple abdominal incisions, and has not shown to be superior to TVT or TVT-O in randomized controlled trials. Cadaveric slings, another surgical treatment option, are used less frequently for a number of reasons, including postoperative pain, voiding dysfunction, lack of durability and rejection issues.

As mentioned previously, the TVT was initially introduced in 1998 as a minimally invasive treatment for SUI. After more than six years of clinical success with TVT, Ethicon launched the TVT-O after years of research and studies performed by the inventor, Professor Jean de Leval, who introduced the inside-out transobturator approach, which differed slightly from Delorme's outside-in approach.

The Instructions for Use (IFU) that accompany the TVT-O device include warnings and precautions to physicians. The IFU emphasizes that physicians should be adequately trained in implanting TVT and should have sufficient knowledge of the pelvic

anatomy to avoid large vessels, nerves, bladder and bowels. The IFU sets out potential risks and complications of the procedure, including the risks of punctures or lacerations of vessels, nerves, bladder or bowel. The IFU warns that a foreign body response may result in extrusion, erosion, fistula formation and inflammation. The IFU warns of the risk of infection and also warns against over-correction (too much tension in the tape). The IFU instructs surgeons on how to place the mesh tension free as follows, "Position the tape loosely e.g. without tension, and flat under the mid-urethra. At this stage a cough test can be performed. This allows adjustment of the tape so that only a few drops of urine are lost during the cough…" The IFU goes on to warn that "Users [pelvic floor surgeons] should be familiar with surgical technique for urethral suspensions and should be adequately trained in the Gynecare TVT Obturator procedure before employing the Gynecare TVT Obturator device."

Further, the IFU mentions that the surgeon should be contacted immediately if dysuria, bleeding or other problems occur. Finally, the risk of de novo detrusor instability is discussed which can occur following sling procedures utilizing the Gynecare TVT-O system. Additionally, the TVT-O IFU warns of transient leg pain that usually be managed with mild analgesics. It is my opinion that the warnings in the TVT-O IFU provided surgeons with adequate and sufficient information about the product and the risks and potential complications at issue. It must be remembered that surgeons gain knowledge from multiple sources, including but not limited to the peer-reviewed medical literature and their clinical experience. My opinions regarding the adequacy of the TVT-O IFU are based on my clinical experience, my review of the medical literature, my

experience teaching medical students, residents, and fellows on the IFU, my review of the FDA's labeling guidance, and discussions with colleagues.

Ethicon also prepared a brochure for patients. This patient brochure can never be a substitute for a meaningful conversation between the patient and her surgeon. This brochure mentions that difficulty urinating, pain with intercourse, scarring and exposure of the mesh can occur. It is the responsibility of any surgeon to ensure that the patient understands the potential risks and benefits of a procedure.

In addition, although it is the responsibility of any surgeon to ensure that he or she is properly trained to perform a procedure, the professional education provided by Ethicon was comprehensive and well-designed. I personally attended formal presentations on the TVT Obturator and Prolift mesh at the Cleveland Clinic Foundation in 2005. This course was given on site at the Cleveland Clinic with their full-time faculty members. The course consisted of didactic lectures on prolapse and associated surgical procedures followed by a cadaver lab where faculty and preceptees worked hands-on to learn these techniques. Instructors told us that we could contact them after the course if we had any specific questions or problems.

In 2004, the TVT-obturator (TVT-O) procedure was introduced as a alternative and less invasive technique to treat SUI. The obturator based approach avoids the retropubic space and trocar passage is easier, as the risk of vascular, bowel and bladder injuries are greatly reduced. This is for several reasons including passage through the obturator space and modifications made to the trocar to make it more narrowed and curved to navigate the obturator foramen. When compared to the pubovaginal sling, the TVT and TVT-O procedures produce superior cure rates at short

term follow up and lower rates of adverse events. Sartori and colleagues (2008) studied 80 patients with SUI. Among those, 61 underwent TVT and 19 a pubovaginal sling. After 6 months, 96.7% of women with TVT and 89.5% of those with a sling thought they were healed from the procedure. Urinary retention was observed in 42% of the pubovaginal sling cases and 9.8% of the TVTs.

All SUI procedures have risks and potential complications; these procedures can and do fail in some patients. All surgeries involve some pain or discomfort and a surgery is never a guarantee of a cure or a pain-free postoperative period. Risks of SUI surgery include anesthesia risks depending upon type, bleeding and transfusion, hematoma, infection, wound complications, urethral injury, organ and nerve damage, voiding dysfunction, urinary retention, urinary frequency and urgency, pain (including pelvic pain), dyspareunia (pain during sexual intercourse), inflammation, scarring, adhesions, urinary tract infections, fistula, DVT and other major surgical risks and need for additional or repeated surgical procedures. These are risks that all urologists, ob/gyns and urogynecologists are trained about in residency and fellowship as well as thoroughly described in the medical literature in a variety of clinical settings, patient types, and levels of surgical experience. These risks do not need to be incorporated in the IFU because they must be considered and are known to any physician who performs pelvic floor surgical procedures. The TVT-O IFU adequately and appropriately warns surgeons of the risks that are related to the clinical use of the device. While suture erosions and graft exposures can occur with Burch and Autologous fascial sling procedures, respectively, mesh erosion and exposure are the only unique complications of synthetic midurethral slings (FDA 2013, AUA 2013).

Pelvic pain, dyspareunia and other pain are frequently found in women of various ages and in the general background populations. I commonly treat women with chronic pelvic pain and persistent dyspareunia who have never had previous surgical treatment for SUI or POP. The causes are multiple, such as other medical conditions like interstitial cystitis, dysmenorrhea, prior surgery, musculoskeletal dysfunction, estrogen status and tissue pliability. The chronic pelvic pain and de novo dyspareunia rates in patients who have received a TVT-O are extremely low. These complications are not new, and in fact, Francis 1961 published on dyspareunia with pelvic surgery, well before the age of pelvic mesh. The medical literature and my clinical experience demonstrate that many women presenting for urologic and gynecologic conditions, such as prolapse and incontinence, have these complaints at baseline.

Urinary incontinence and pelvic floor prolapse can be associated with sexual dysfunction. Affected patients can complain of difficulty with sexual desire, arousal, orgasm, lubrication, pain and satisfaction. Risk factors for female sexual dysfunction include: post-menopausal status, degree of pelvic prolapse, concurrent medical problems such as hypertension, diabetes and thyroid disease, surgical menopause from hysterectomy and scarring from prior episiotomy and repair of tears during childbirth. Pelvic pain and other pain (inguinal and lower extremity related pain) is a known risk of sling procedures (or any other vaginal surgery). However, pelvic pain, dyspareunia, and other sexual function factors such as fear of sex from incontinence, can also improve after sling procedures. Of course, there are patients who have pelvic pain in addition to urinary incontinence and desire their incontinence treated. In the appropriate patient with urethral hypermobility and documented stress urinary incontinence, a TVT can be

considered a first line treatment. Such patients may achieve a cure of their stress incontinence while their pelvic pain worsens. In my experience, this worsening of pelvic pain following TVT is unrelated to the TVT but rather is due to pelvic floor neural hypersensitivity. These patients with chronic pain and stress incontinence who desire a TVT (or another surgical treatment for incontinence) are warned about the possibility of worsening of pelvic pain after the anti-incontinence procedure.

Another potential complication of synthetic sling procedures is the risk of mesh exposure or erosion. This uncommon complication can usually be treated very easily. The FDA has noted the mesh exposure rate for synthetic midurethral slings to be around 2%. (FDA 2013). This is consistent with larger reviews of the medical literature (Tommaselli 2015, Schimpf 2014, Novara 2008, Ford 2015, Unger 2014, Jonsson-Funk 2013, 2013, Nyguen 2012). Long-term studies evaluating the TVT-O have shown consistently low exposure rates over time, which suggests that most erosions or exposures occur within the first 12 months. Surgeon technique and volume also plays a significant role in the incidence of complications. (Welk 2015). Welk and colleagues also discussed how most of the patients in their large population study who experienced a complication return to the implanting physician, which is contrary to a small tertiary study by Abbott (2014). In this latter paper, the authors noted that 50% of patients who sought treatment for a mesh complication at a tertiary care facility actually had their procedure performed at a different facility. The risk of erosion associated with sling procedures was well known among pelvic floor surgeons since their inception with the original TVT in 1998 and in fact before that as the medical literature reported on the use of synthetic materials to surgically treat SUI as well as potential complications including

mesh exposure and erosion. In addition, all pelvic floor surgeons understand from their training and experience that no treatment is guaranteed to cure SUI and complications can always occur.

It is important to discuss cytotoxicity with regard to mesh based slings. Wang (2004) reported a 2.4% rate of defective vaginal healing and a 1 % incidence of persistent delayed healing of the anterior vagina, 1 to 7 years after the operation. They believe that vaginal erosion may occur after delayed infection of the synthetic sling or prominent foreign body reaction, which leads to separation of the vaginal incision and sling erosion. In their study, six women had complete epithelialization over the mesh after 1 debridement of the vaginal tissue. They attribute these results to the presence of factors such as inadequate vaginal tissue coverage during the operation, rigidity of the mesh and its propensity for injury to adjacent tissues, or a site-specific, localized inflammatory response of the suburethral vagina is also plausible. This latter theory is important to note because in patients with complete epithelialization of the mesh who later had removal for other reasons, several patients displayed evidence of foreign body reaction, dense fibrosis, and occasional perivascular mononuclear cell infiltration. Thus, the inflammatory histologic reaction associated with slings can be present in slings that have extruded, have epithelialized or appear completely normal upon examination.

Carcinogenesis has become another important point worthy of discussion. King (2014),Moalli (2014), and Linder (2016) reviewed the incidence of malignancy associated with pelvic mesh. No reports of malignancy have been reported in humans directly associated with these slings. The FDA, AUGS, and SUFU all have reported that midurethral slings are safe and effective. We all believe that continued research is

necessary but should be done in a scientific fashion to ensure its validity. As of this writing, there is no evidence to suggest that polypropylene midurethral slings have any association with malignancy.

Given the current discussions regarding synthetic mesh versus absorbable sling materials, it is logical to consider a partially absorbable mesh for the treatment of stress urinary incontinence. Okulu (2013) evaluated complication rates of mixed types of mesh materials over a 4 year period in 144 women with SUI. They utilized Vypro (semi-absorbable multifilament plus absorbable polyglactin), Ultrapro (semi-absorbable monofilament + nonabsorbable polypropylene) and compared that to Prolene light mesh. All three groups exhibited similar continence rates at four years follow up. Interestingly, vaginal erosions of mesh were noted in all groups as were urethral erosions of mesh. De novo urgency and incontinence were also observed in all groups. In 2010, Ethicon considered Ultrapro as a novel concept for slings but the sterilization process made the Ultrapro stick to the side of the sheath and caused the mesh to stretch out (DX 23551.1, Elbert R&D Memorandum 12.2.2012). Further, in a SCION PA/SUI Treatment Unmet Needs Research Panel 1.22.2010, roughly 65% of physicians believed that partially absorbable mesh would not have any potential benefits. Further, they would want to see at least 2 years of clearly beneficial efficacy data before considering this potential treatment. Many are concerned that the use of a partially absorbable mesh is like the worst of two worlds. The sling will be weaker because of absorption and there is still the presence of synthetic material in the body. Finally, in a letter from the FDA to Ethicon on December 21, 2010, this device was rejected by the FDA because if lack of superiority to current available products (TOPA TVTO-PA 510K

Rejection Letter).

Laser Cut versus Mechanically Cut Mesh has become another important topic of discussion. I have only had three patients with mesh extrusions over a 15 year period and could not tell the difference between either mesh variation until I looked closely at the mesh with as magnifying glass. Personally, I have not seen any difference in complication rates between either variation of mesh in my clinical practice or in the peer-reviewed medical literature. In the many cases of urethrolysis I have performed over the years, I have not removed degraded particles of mesh or seen grossly altered structure of the knitting of the mesh in any of these specimens.

Multiple studies and professional society consensus statements, surveys, and clinical practice guidelines, including but not limited to AUGS, SUFU, AUA, IUGA, NICE, EAU, and ACOG, have confirmed that midurethral synthetic slings are the treatment of choice and the standard of care for the surgical treatment of SUI. The 2014 AUGS and SUFU position statements highlight three important facts about synthetic mid urethral slings. (1) Polypropylene material is safe and effective as a surgical implant. (2) The monofilament polypropylene mesh MUS is the most extensively studied anti-incontinence procedure in history. (3) Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients. Similarly, the AUA released a position statement approved by the Board of Directors in 2011 and revised in 2013, stating in part, "Extensive data exist to support the use of polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain,

reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well."

E. Pertinent Outcome Data available to all physicians who perform TVT and TVT-O procedures. Considerations for discussions with patients in the pre- and post-operative period.

Since the introduction of the TVT in 1998 and TVT-O in 2004, there have been hundreds of RCTs and thousands of other papers reporting the safety and efficacy of these procedures which utilize the same Prolene mesh, including numerous long-term studies. These papers have also been presented in regional, national and international meetings as well as CME conferences both live and on-line, and are often delivered to doctors' offices from various journal subscriptions. Similarly, papers have been presented and published regarding the challenges with the procedure, follow up and patient selection. It is the responsibility of each implanting physician to be up to date regarding new data pertinent to their practice. Of particular importance is the relevance of preoperative voiding symptoms, the role of multiple pelvic surgeries performed at the same time in addition to sling and sexual pain unrelated to the mesh itself.

Regarding the relevance of preoperative voiding symptoms, patients who only have stress incontinence do best when a sling is performed. However, patients with mixed UI tend to do worse. Aigmueller (2011) reported a 10 year follow up of patients after TVT procedure studying 117 patients. Subjectively, 6.4% considered themselves to

be unchanged and 11% considered themselves to be worse in terms of their leakage after sling. They reported that 37% of patients with preoperative mixed urinary incontinence still had urge urinary incontinence post operatively. Their reported rate of detrusor instability was 20%. This data was similarly reproduced by Svenningsen and associates (2012) who reported that 23% of patients had subjective voiding difficulties and denovo urinary incontinence increased from 4.1% after surgery to 15% at 10 year follow up. Groutz in 2011 reported that patients who had surgical treatment failure after sling procedures are more likely to have recurrent UTI and post operative incomplete bladder emptying. In another paper by Groutz (2011), preoperative detrusor overactivity was reported as an independent risk factor for sling failure. Aigenmueller (2014) looked specifically at reasons for dissatisfaction with sling procedures. They noted that 15% of patients were worse after their sling. This was most prevalent in patients with preoperative urge urinary incontinence. The authors go on to suggest that patients should be counselled that if they have mixed urinary incontinence and recurrent UTI preoperatively that they are at higher risk for failure of their sling and dissatisfaction in the results of their surgical procedure. The abovementioned papers are significant and these results mentioned to at risk patients prior to and after performing sling procedures at each office visit with the patient. Of note is that all of these factors were present in Ms. Guinn preoperatively such that her post operative course is not surprising.

The risk of performing multiple surgical procedures at the same time must also be considered by the operating surgeon. If a surgeon is considering a hysterectomy, prolapse repair and sling, the risk of all of these procedures should considered as potentially additive and a detailed discussion with the patient must be undertaken.

Abdelmonem (2010) evaluated the vaginal length and dyspareunia after TAH and TVH. Postoperatively, there is a significant decrease in vaginal length by approximately 2 cm in the TVH group. This is statistically significant when compared to no loss of length in the TAH group. There is a significant increase in dyspareunia in the TVH group as compared to the TAH group. The authors theorize that this decrease in length is due to redundant trimming of the vaginal wall during vaginal prolapse repair. Further, Athanasiou (2014) reported on the 7 year follow up of outcomes of TVT-O. The authors found that when multiple procedures are combined that the subjective cure rate for incontinence was lowest. Specifically, when TVT-O is performed as the sole procedure, 90% of patients have an objective cure rate. However, when hysterectomy is combined with pelvic floor reconstruction and TVT-O sling procedure, the objective cure rate decreases to 74%. Of note is that Ms. Guinn had a TVH, BSO, prolapse repair and TVT-O sling. Thus, it is not surprising that she has a higher rate of subjective failure of her sling.

Finally, it is known to all surgeons who perform pelvic floor surgery that there are significant risks of sexual dysfunction post operatively. While the literature and patient brochure mentions that sexual intercourse pain can result, there are important inherent risks of pelvic surgery that must mentioned to all patients. Tucker (2015) reported in 119 patients who underwent risk reducing salpingo-oopherectomy. Of these 119 patients, 72% underwent concomitant hysterectomy. They found that 74% of patients had postoperative sexual dysfunction including 44% with lubricating difficulty, 41% with reduced sexual satisfaction, 28% with dyspareunia and 28% with orgasm difficulty. Thus, the risks of not only dyspareunia but the entire spectrum of female

sexual dysfunction must be discussed with all patients who undergo any type of pelvic floor surgical procedure.

Ms. Guinn's History, Treatment with review of pertinent depositions

Susan Guinn is a 63 year-old gravida 3 para 3 woman with a long history of uterine prolapse and cystocele. She has been seen by Dr. Warren Cooper since approximately 2001. She complained of pressure symptoms and wanted to proceed with definitive surgery. She also noted a history of urinary urgency requiring medical treatment with multiple anticholinergic agents including Ditropan, Detrol and Vesicare. Per the History and Physical Examination from 4/7/2010, Dr. Cooper noted that "she denies any stress incontinence but does have some urgency incontinence for which she takes Detrol to control...(he) explained to her that while (we) will be repairing the cystocele and placing a sling to prophylax against the development of stress incontinence she probably will still need to be on the Detrol after the surgery. She understands and agrees." Pelvic examination at that time revealed a 2nd to 3rd degree cystocele with a parous cervix with second degree desencus. The uterus was of normal size and shape. No adnexal masses were appreciated. There was no mention of stress incontinence on the physical examination. Dr. Cooper's plan was LAVH, BSO, anterior repair and TVTO sling procedure. According to the deposition transcript of Dr. Cooper, he stated that he gave the patient a Mesh brochure which mentioned risks of the surgery including difficulty urinating, mesh material exposure within the vaginal wall and sexual pain. The patient brochure in effect from 2008 to 2010 (Eth.Mesh.080003279) discussed the following risks:

> "All surgical procedures present some risks. Complications associated ith the procedure include injury to blood vessels of the pelvis, difficulty urinating, pain, scarring, pain with intercourse, bladder and bowel injury. There is also a risk of the mesh material becoming exposed. Exposure may require treatment…. Synthetic mesh is a permanent medical device implant. Therefore, you should carefully discuss the decision to have surgery with your doctor and understand the benefits and risks of mesh implant surgery before deciding how to treat your condition."

It is noteworthy to mention that Dr. Cooper was aware of the 2005 IFU that stated that the TVT sling is "to be used in women as a sub-urethral sling for treatment of stress incontinence (SUI) resulting from urethral hypermobility and/or intrinsic deficiency." As mentioned above, this patient, at the time of her 4/7/2010 office history and physical examination with Dr. Cooper demonstrated no subjective or objective signs of SUI. She had no evidence of stress urinary incontinence on examination. A Q-tip test was not performed nor was there evidence of urethral hypermobility on examination. In Dr. Cooper's deposition he "…talked about doing the thing (sling) to help against the development of stress incontinence……(continues)…..make sure she does not come back 6 months later with worsening SUI that needed a sling at that point in time." He further stated that "it is a good idea to perform a sling if there is hypermobility." However, his examination prior to surgery did not indicate that she had such finding.

The patient underwent laparoscopic assisted vaginal hysterectomy, bilateral salpingo-oophorectomy, anterior colporrhaphy and TVT [TVT-O] with sling procedure on 4/23/2010 by Dr. Cooper. Review of the operative note notes no complications and an estimated blood loss of 20 cc. Of additional note is that Dr. Cooper did not perform an apical repair at this time. It is well known that recurrence after prolapse often occurs in the apical compartment when it is not repaired at the time of initial surgery. At follow up visits within 6 months of surgery, the patient complains of recurrence of per prolapse which is likely in the apical compartment. Ms. Guinn stated she was having painful urination on 5/19/2010 and urine culture was sent which revealed greater than 100,000 CFU of E.coli. She was seen post operatively on 5/26/2010 and noted improvement in her bladder symptoms. Examination revealed the bladder sling to be in position and well suspended. Urine dip was negative and the patient was started on Detrol LA. Positive urine cultures were also noted on 7/15/2010. Follow up office examinations by Dr. Cooper on 7/20/10 and 7/26/10 revealed less urinary burning and requency. Examination on 7/26/10 revealed the sling to be in good position. Patient will continue her Detrol LA. She went to see Dr. William Cartwright (PCP) 10/1/2010 for persistent dysuria. He did not perform a pelvic examination but noted that she had 2 culture positive UTIs since her surgery on 4/23/2010 (thus, 2 infections in a 6 month period). Subsequent urine cultures of 10/1/2010, 10/21/2010, and 11/1/2010 failed to show significant evidence of a UTI. Removing Ms. Guinn's ovaries reduced her estrogen levels which will potentially increase her risk of UTIs. Given this pertinent history, she would benefit from topical estrogen therapy. A 2014 systematic review by the Society of Gynecologic Surgeons

found that postoperative vaginal estrogen use after a midurethral sling resulted in decreased urinary frequency and urgency.

On 11/15/2010, Ms. Guinn saw Urologist Dr. David Mendoza for persistent dysuria. UA at that time was negative for nitrates and leukocytes. Laboratory studies revealed a normal serum creatinine. Ultrasound of the bladder on 11/19/2010 revealed "the initial bladder volume was calculated at 170 ml and the post void residual is calculated at 130 ml." Patient was informed of these findings which indicate that she only eliminates approximately 30% of her bladder volume. Of note is that no preoperative urodynamics were performed on Ms. Guinn prior to her original surgical procedure. Given the lack of UTIs prior to her initial surgery, one can assume that her bladder emptied relatively completely. Thus, the reason for the elevated PVR above after surgery is likely due to the placement of a suburethral sling in a patient with no urethral hypermobility and a normal urethral to bladder axis. Thus, sling position in such a patient can result in urethral narrowing (perceived as urethral stenosis). On 12/6/2010, Ms. Guinn underwent cystoscopy, urethral dilation, bilateral retrogrades and vaginal examination under anesthesia by Dr. Mendoza. Findings from the operative note revealed:

- Grade 1-II cystocele
- Bladder revealed no foreign bodies, tumors, stones or obstruction
- The urethra was stenosed/tight.
- The urethra was dilated using female urethral dilators to 26 Fr without difficulty
- She had a somewhat short vaginal orifice

- She had a grade I-II cystocele as well as some grade 0-1 rectocele and her cuff did not appear to be secured.
- Consideration was suggested to anterior repair was suggested by Dr. Mendoza although he noted that this may worsen her rectocele or even develop an enterocele

The operative note does not mention any evidence of sling extrusion or erosion. As mentioned above, this patient did not have evidence of stress urinary incontinence at the time of her hysterectomy/prolapse repair. She had a sling performed to prevent prophylax against stress urinary incontinence. The sling procedure is not supported by the IFU as the patient does not have stress incontinence. The IFU states that TVT-O is "intended to be used in women as a sub-urethral sling for the treatment of stress urinary incontinence (SUI) resulting from urethral hypermobility and/or intrinsic sphincter deficiency." When a sling is performed in a patient who does not exhibit stress incontinence, there is not usually urethral hypermobility. Thus, the sling, even when placed according to the surgical guidelines, it can compress the urethra and create voiding dysfunction. This can be evidence by recurrent UTI and elevated post void residuals. As noted above, this patient, by ultrasound measurement only empties 30% of her bladder volume. Further, Dr. Mendoza noted that the urethra was stenosed/tight on examination and performed urethral dilation to attempt to relieve this obstruction. As for the vaginal shortening noted by Dr. Mendoza, this is most likely to be due to the combination of several factors including her hysterectomy, anterior repair and the presence of an enterocele. In my experience, slings are not known to shorten the vaginal canal in the absence of obvious sling erosion or extrusion.

The patient was again seen by Dr. Mendoza in follow up after the above procedure on 1/20/2011. Her biggest problem at that time was leaning forward to void and some urgency. No pelvic exam was performed. Given the studies performed by Dr. Mendoza and the multiple examinations performed. He did not recognize that the sling was causing the obstructive symptoms seen in this patient. While he correctly treated her initially with urethral dilation, when he saw her back in follow up and noted that she had to sit forward to void, he could have considered urethrolysis given that a sling was placed in patient without SUI or urethral hypermobility on examination and that is the most likely cause of her current symptoms. Gynecologic follow up by Dr. Cooper on 7/6/2011 noted a normal pelvic examination without mesh extrusion. Urine culture at that time failed to show a UTI. She was seen by Dr. Cartwright on 9/24/2014 complaining of 2 weeks of dysuria. Urine culture revealed an E.coli UTI. No pelvic examination was performed.

Of note is that Ms. Guinn has not had her sling removed or revised. She stated in her Plaintiff Fact Sheet and other forms that she attributes the outcomes of pain, urinary problems and infection to the device. She states that "frequent UTIs, urinary retention which required urethral dilation." Only one such urethral dilation was performed and no other measurement of bladder function other than an initial ultrasound was performed. Further, on review of the office notes from 4/14/10, 7/20/10, 7/26/10, 11/15/10, 12/6/10, 1/20/11, 7/6/11, 9/24/14 there is no mention in the record of any complaints of "pain" that Ms. Guinn complained of. The complaints of urinary problems and infection have been mentioned in the record. Of note is that the patient brochure

provided to Ms. Guinn stated that difficulty urinating, pain, scarring, pain with intercourse, bowel and bladder injury could occur with the procedure. These are risks of any pelvic floor surgery that the implanting physician would and should know about. In her deposition, Ms. Guinn stated that Dr. Cooper did explain the risks of the surgery and she would not disagree that he did indeed do that. She also stated that she did receive brochures prior to the procedure for the sling and possibly the hysterectomy procedure. She does not have any recollection of signing informed consent for the surgical procedures.

With regard to her treatments by Dr. Mendoza, she does remember seeing him and stated in her deposition that she still is having UTIs and is "not sure how many." She has had no other urologic procedures. She admits to pulling in her groin that "happens once in a while." She has not spoken with any of her physicians about the pain and stated "…I guess I have it, then I do not have it (pain)…" She voids 10/day and 1-2/night. With regard to UTIs, she stated in her deposition that she makes no special attempts to prevent UTIs. She "drinks a lot of water" and goes on to say "I am not aware of anything else to do about them."

Rebuttal of Expert Witness Deposition Testimony:

In review of the Expert Witness Report of Dr. Rosenzweig, the following comments are made:

- Dr. Rosenzweig notes …. "In coming to those conclusions, a broad differential diagnosis was reviewed and considered including her medical history, which includes: ….uterine prolapse, cystocele, frequency, stress urinary incontinence,

urgency, ……None of these factors increased the risk for developing her symptoms." (Rosenzweig, Expert Report page 13). This opinion is not true. As previously cited above, Abdelmonem (2010) and colleagues noted that pelvic floor surgery is associated with significant risks of decreased vaginal length and post operative dyspareunia. Further, Athanasiou (2014) noted that when multiple procedures are performed at the same setting that there is a decrease in the success rate from the sling procedure. Thus, these considerations certainly play a role in the post-operative complaints of Ms. Guinn.

- Dr. Rosenzweig notes "As a result of the implantation of the TVT-O transvaginal mesh product, including the mesh characteristics discussed below, and the subsequent reactions and surgical revisions, Ms. Guinn has sustained the following injuries, which are most likely permanent in nature: frequent urinary tract infections; dysuria radiating into the lower back; recurrent frequency; recurrent urgency; recurrent nocturia; urinary retention; difficulty emptying the bladder, requiring her to bend forward to void; and a pulling in her groin on the inner thigh crease. (Rosenzweig, Expert report page 13). This opinion is false on multiple levels. First, Ms. Guinn has not had any "subsequent reactions and surgical revisions" as stated above. She simply had sling placement at the time of her hysterectomy. She has not had any signs on physical examination to suggest mesh erosion or extrusion. She has not had any subsequent procedures to remove the mesh nor has any of her treating physicians suggested that the mesh was the cause of her symptoms. With regard to the pulling in her groin on the inner thigh crease. Ms. Guinn has not mentioned this complaint to any of her treating

physicians and in her own deposition references the pain as coming and going describing an intermittent pain that has little if any impact on her life.

- Dr. Rosenzweig states "to a reasonable degree of medical and scientific certainty, that the debilitating injuries suffered by Ms. Guinn, which are listed above, were directly caused by the TVT-O transvaginal mesh device, including the following polypropylene mesh characteristics: (a) degradation of the mesh; (b) chronic inflammation and chronic foreign body reaction; (c) mesh that was never meant to be implanted inside the human body and is incompatible with peroxides and the naturally occurring condition of a woman's vagina and pelvic floor; (d) deformation, rigidity, fraying, roping, cording and curling of the mesh; (e) loss of pore size with tension; (f) fibrotic bridging leading to scar plate formation and mesh encapsulation; (g) shrinkage/contraction of the encapsulated mesh; and (h) the difficulty and/or impossibility of removing the devices. (Rosenzweig Expert Report, page 14). These statements have no relevance to Ms. Guinn. As stated above, Ms. Guinn has had no signs or symptoms of mesh erosion or extrusion on physical examination by any of her treating physicians. Further, none of her treating physicians has suggested that she have her mesh removed. Finally, given that her mesh is still in-situ, there is no way of knowing that any of the abovementioned polypropylene mesh characteristics have any role in Ms. Guinn's condition. Unless her mesh is removed and analyzed for its specific role in her symptoms, the abovementioned generalized characterized mesh statements have no relevance to the present case.
- Dr. Rosenzweig goes on to describe additional irrelevant characteristics regarding

Ms. Guinn's mesh "…..to a reasonable degree of medical certainty, contraction, shrinkage, deformation, degradation, and rigidity of the TVT-O, the materials used to manufacture the TVT-O, and the design of the TVT-O, or a combination of these factors, caused Ms. Guinn's injuries." (Rosenzweig Expert Report, page 14). Again, for the reasons described above, since this patient has not had removal of her mesh, these statements have no relevance to the symptoms noted by Ms. Guinn.

- Dr. Rosenzweig make comments about Ms. Guinn's groin pain "...Groin Pain: Prognosis is poor. It is highly unlikely, even with medication use, aggressive physical therapy, biofeedback and/or surgical intervention, for Ms. Guinn to have complete resolution of the groin pain." (Rosenzweig Expert Report, page 15). This information as stated by Dr. Rosenzweig is incorrect. If the groin pain exhibited by Ms. Guinn were significant, she would have mentioned it to her treating physicians. She has not done so in review of her medical records. Further, in her own deposition, she goes on to say that "happens once in a while." She has not spoken with any of her physicians about the pain and stated "…I guess I have it, then I do not have it (pain)…" Multiple long-term studies, Cochrane reviews, meta-analyses, and randomized controlled trials have demonstrated how long-term groin pain after TVT-O is rare.
- Dr. Rosenzweig notes "Urinary Dysfunction (frequent urinary tract infections; dysuria radiating into the lower back; recurrent frequency; recurrent urgency; recurrent nocturia; urinary retention; and difficulty emptying the bladder, requiring her to bend forward to void): Prognosis is poor. It is highly unlikely,

even with medication use, aggressive physical therapy, biofeedback and/or surgical intervention, for Ms. Guinn to have complete resolution of the urinary dysfunction." (Rosenzweig Medical Report, page 15). The prognosis of Ms. Guinn's voiding dysfunction is actually quite good if she receives appropriate treatment. First, as stated previously, Ms. Guinn had a sling placed without evidence of urethral hypermobility and SUI on her examination immediately preceding her hysterectomy, anterior repair and sling procedure. Placing a sling in a patient without SUI is not indicated according to the IFU. When slings are placed in such patients, there is a significant risk of post operative voiding dysfunction. This was not recognized by any of her treating physicians although it was clearly mentioned by Dr. Cooper in his preoperative history and physical examination where he acknowledged that Ms. Guinn did not have SUI and was placing the sling to prevent incontinence. Actually, if Ms. Guinn undergoes urethrolysis, she has an excellent chance, in my experience, of seeing significant improvement in her bladder emptying and rate of UTI development.

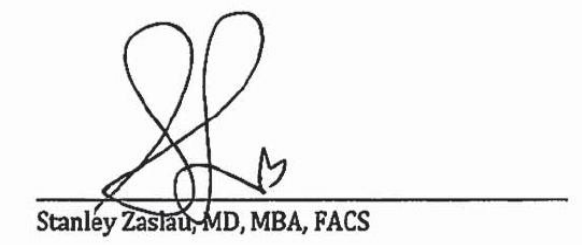
- Finally, Dr. Rosenzweig opines that "Dr. Warren Cooper's treatment of Ms. Guinn met the standard of care. The pre-operative evaluation of the patient met the standard of care. The implant procedure was indicated due to complaints of stress urinary incontinence symptoms and was performed within the standard of care with no evidence of surgeon error or deviation from the procedural steps. There was no evidence of any surgical complications, excess blood loss, excess surgical duration, or surgical site contamination in the records." (Rosenzweig Expert Report, page 12). This assertion is incorrect. The IFU clearly states that slings

are indicated in the treatment of SUI due to urethral hypermobility. This patient does not have evidence of either SUI or urethral hypermobility. Placing a sling in such a patient without SUI can certainly be associated with significant morbidity. If the IFU was the only document a surgeon relied upon, then, for example, in this case the surgeon should not have even used TVT-O because Mrs. Guinn did not have proven SUI prior to the surgery. While there is literature reflecting good treatment outcomes through the use of a prophylactic midurethral sling, using a midurethral sling prophylactically is a judgment call of the surgeon and cannot be blamed on the manufacturer's IFU when known complications occur thereafter.

Conclusions:

From the review of the medical records and deposition transcripts, there is no objective or subjective evidence to suggest that the mesh characteristics of the TVT-O sling are the cause of Ms. Guinn's voiding issues. Her sling was appropriately placed in the surgical procedure with no subsequent findings of erosion or extrusion. However, the sling was placed without proper guidance from IFU which explicitly states that slings should be used in the management of SUI. At the time of surgery, Ms. Guinn had no subjective or objective evidence of SUI. When slings are placed in the absence of urethral hypermobility, they are more prone to cause voiding difficulties in patients as evidence by straining to void, positional voiding, elevated post void residuals and recurrent UTIs. These are the findings seen in Ms. Guinn. The IFU is not to blame for Ms. Guinn's complaints. The complications she experienced are well-known complications of sling placement, although they are more commonly seen with retropubic

slings as opposed to transobturator slings given the approach, and are warned about in the IFU and Patient Brochure.



DATE

Attachments:

CV
Reference List